9. Mention is made of a difference in the response to the roentgen-ray of the leukemic and the granuloma groups as seen in the affected lymph node. This will be taken up in a later communication.

10. An attempt at the production of an antigen for specific protein skin tests in the lymphatic diseases resulted negatively.

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THE HEART IN INFECTIOUS DISEASE.[1]

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One of the most interesting and puzzling questions in the practice of medicine is the effect of infectious disease on the heart. Much unwarranted empiricism still exists in the treatment of the circulation during and after an infection. It is well now and again to pause and to take account of the progress of our knowledge of the influence of infectious disease on the heart and circulation. It is my desire to call attention to some of the known facts of this influence and to urge investigation of points that are in doubt. I shall take up in turn briefly the pathology, symptomatology and treatment of the heart in infectious disease.

In discussing the changes in the heart due to infections it is necessary to separate these infections into two groups: First there are those diseases which are quite likely to cause some permanent damage to the heart, and, second, there are infectious diseases in general which poison the heart temporarily but probably result in little or no permanent damage. In the former group are, in the first place, the infections of the rheumatic type—rheumatic fever, chorea, tonsillitis and scarlatina; secondly, there is diphtheria; thirdly, syphilis; and finally, the diseases, such as pneumonia, influenza and streptococcus septicemia, which may rarely attack the heart directly. Temporary poisoning of the heart muscle may result from almost any disease—typhoid, pneumonia and so on.

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[1] Read before the Section on General Medicine of the College of Physicians of Philadelphia, March 28, 1921.

Rheumatic fever and allied infections may attack and produce changes in endocardium, myocardium, and pericardium, any one, two, or even all three. A pancarditis is not uncommon. The typical lesion is the Aschoff body, or submiliary nodule, in the myocardium. Extensive involvement of the myocardium would result in considerable scarring so that permanent damage must always be suspected in the heart of any patient during or after illness belonging to this rheumatic group. The valves or pericardium give evidence of extensive cardiac involvement in rheumatic fever. Rarely if ever is the myocardium much damaged without evidence of endocardial or pericardial disease also, although transient heart-block may occur in rheumatic fever in hearts which do not show signs of valve changes or pericarditis. The occasional finding of acute heart-block should make one feel that any person who has suffered from rheumatic fever is not likely to have a perfectly normal heart even though it appears normal to auscultation and percussion.

Diphtheria toxin may produce serious and extensive necrosis of the myocardium, and here again it seems likely that any person who has been through a severe attack of diphtheria has a scarred heart. Heart-block, sometimes of very high grade, has long been known to occur in diphtheria. In my cardiac clinic are two cases of complete heart-block in young people whose past history is negative except for diphtheria. Not only may there be extensive auriculo-ventricular block, but also intraventricular block of bundle branch and arborization type may be found. How often such changes may occur transiently in diphtheria we are beginning to discover. Finally there is one other cardiac condition of great importance in diphtheria—that is, the sudden collapse with gallop rhythm, leading at times to sudden death and ascribed to cardiac nerve involvement ("disintegration of the vagus," as Park calls it). This condition needs further study.

Syphilis affects the heart in two ways: either directly by gummatous invasion of the myocardium or by arteriosclerotic changes in the aorta and coronaries, or by both. Syphilitic aortitis is beginning to be regarded generally less as a disease entity and more as a condition associated with cardiac syphilis. In other words, one may speak rather of syphilitic heart disease with aortitis than of aortitis alone. There may be extensive syphilitic involvement of the bundle of His and its branches which yields to antisyphilitic treatment, or there may be thromboses with scarring of the myocardium, perhaps leading to aneurysm of the heart itself and perforation of a ventricular wall. Any patient with chronic syphilis should have a careful investigation of heart and aorta made—by examination, roentgen ray and electrocardiogram. How early in the disease the heart may be attacked we are not yet sure. Undoubted cases of secondary syphilis with cardiac involvement are on record, and Brooks[2] thinks that it may be common. At the Massachusetts General Hospital we have been examining secondary syphilitics from the cardiac standpoint, but as yet have failed to find out of a small number any giving signs or symptoms of cardiac involvement. It seems likely that such invasion may occur early in lues without any evidence.

Other rarer infectious causes of permanent damage in the heart are such diseases as pneumonia and typhoid fever. Rarely an endocarditis or a pericarditis may result from pneumonia, and the myocardium itself in fatal cases may show cloudy swelling and necrosis. Postmortem examination of typhoid fever hearts shows not infrequently mottling with marked parenchymatous degeneration microscopically. It is unlikely, however, that mild attacks of typhoid fever produce much change. The blood-vessels, both arteries and veins, may be considerably damaged in typhoid fever, and this disease has been included by some as a likely cause of arteriosclerosis. Other diseases such as influenza, gonorrheal septicemia and streptococcus infections may rarely result in endocarditis, pericarditis or perhaps myocarditis.

Now let us turn to infections as they affect the heart temporarily by poisoning. One of the most important papers of recent years is that of Newburgh and Porter.[3] They wrote as follows: "The experiments consist of four series of ten dogs each. In the first the normal ventricle was fed with normal blood; in the second the pneumonic ventricle was fed with normal blood; in the third the normal ventricle was fed with pneumonic blood; in the fourth the pneumonic ventricle was fed with pneumonic blood.

"It is very generally believed that the heart muscle is seriously injured in pneumonia and that heart failure from this source is a frequent cause of death in this infection.

"The experiments presented in this communication show that the cardiac ventricle from dogs that have died from pneumonia contracts as well as the ventricle from healthy dogs, provided the pneumonic muscle is fed with normal blood. When a normal ventricle is fed with pneumonic blood the contractions are much impaired. If, however, the ventricle from a dog with pneumonia is fed with pneumonic blood the contractions are almost normal in extent and may be normal in duration.

"Thus in pneumonia the heart muscle is essentially normal, whereas the pneumonic blood is distinctly poisonous to heart muscle suddenly fed with it. In the body, during the gradual course of the disease, the blood is progressively affected and the heart muscle gradually adjusts itself to the poison, with striking success."

The effects of poisoning of the heart resulting in functional incapacity when severe, disappear with recovery from the infectious disease or very soon after. At times, without doubt, there is a combination of permanent destructive action and temporary poisoning in the same heart during such an acute infection as rheumatic fever. It is in such a case that one finds the greatest difficulty at the time of the infection in the presence of fever, in gauging how much involvement is transient and how much permanent.

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[2] Syphilis of the Heart Read at a meeting of the Suffolk District Medical Society, Boston, December 29, 1920.

[3] Jour. Exper. Med., 1915, 22.

The symptoms and signs of actual cardiac damage in acute infectious disease are very few. Precordial pain, dyspnea and palpitation are suggestive and always attract one's attention to the heart, but severe involvement of the heart may occur without any of these. What is more, these symptoms may be nothing more nor less than evidence of irritable heart, effort syndrome, cardiac neurosis or whatever one wishes to call it. There is, I believe, no pathognomonic symptom of cardiac involvement in infectious disease. I desire particularly to emphasize here the tendency for such effort syndrome symptoms to appear, or, if already present in an individual, to increase during an infection and during convalescence from it. Not only easily acquired dyspnea and palpitation, but also early exhaustion, faintness, dizziness, sweating, and tremor come on with very little effort in one suffering from acute infectious disease or still weak from the effects of it in convalescence. Every one of us who has suffered from some infection will remember these distressing symptoms if he has tried to work through the course of the infection, or at least at the beginning of it, before forced to go to bed, or if he has started to work too soon during his convalescence. This was seen widely during the influenza epidemic, but it is common in all kinds of milder illnesses such as tonsillitis, colds and gastro-intestinal upsets with fever. Notwithstanding this association one finds very often that medical men regard these symptoms as evidence of heart damage and begin to fill the patient with the so-called stimulants. Common-sense is needed not infrequently in the treatment of such cases, and drugs can largely be scrapped.

The effort syndrome of acute infectious disease, which may occur without any more effort than that of the struggle of the organism against the disease, may be ascribed to one of two causes, or often to both. At the beginning of an infectious process toxemia may be blamed for the symptoms, later on both toxemia and exhaustion play a part, and finally the exhaustion factor holds sway during convalescence.

During the war the attempt at times was made to ascribe all effort syndrome to low-grade infection in progress or to the effects of a recent acute infection. Undoubtedly these causes did figure frequently in the production of the syndrome in the armies, but often simply exhaustion, usually in a nervous man, was the cause. Here, again, our war experiences are useful to us, for this syndrome found in the tired soldier may be compared directly with that found in the sick civilian.

The signs of actual cardiac involvement in infectious disease are more definite than the symptoms. The development of diastolic murmurs, of marked systolic murmurs with thrills, of pericardial friction rub or signs of effusion into the pericardium, of heart-block and perhaps of auricular fibrillation or flutter, and finally the signs of heart failure of the congestive type (edema of the lungs, over the sacrum and in the extremities)—the appearance of any of these signs is evidence of actual cardiac involvement. Systolic murmurs, cyanosis, questionable increase in heart size to percussion, premature beats, small, weak, dicrotic or rapid pulse are by no means evidence of cardiac involvement; they are much more liable to be due to general functional disturbance of the circulation, possibly with myocardial weakness and irritability, but not due to actual myocardial disease. Tachycardia is a common response of the nervous mechanism of the heart to fever and toxin—a sympathetic stimulation. The rate of the pulse varies in different diseases in the same individual—for example, high in pneumonia and relatively low in typhoid—and in different individuals with the same disease. There is a general tendency for most toxins to produce a tachycardia. Occasionally, as with mumps, one finds a relatively slow pulse quite generally. But also it must be remembered that individuals may react very differently to the same disease; in some a much faster tachycardia occurs than in others. Children particularly are susceptible to such tachycardias. Hence a rapid tachycardia, *per se*, must not be taken as evidence of disease of the heart resulting from the infection itself—it may be merely a given individual's reaction to the poison. Likewise, after the infection is over—in convalescence—a bradycardia may be an individual characteristic and not evidence of heart disease.

I should like to add a word here about so-called acute dilatation in acute infectious disease. Undoubtedly at times these impressions are based on uncertain percussion data, sometimes on the onset of an unusual cardiac mechanism such as paroxysmal auricular fibrillation with actual cardiac failure if long continued, and once in a great while a rapidly developing pericardial effusion will simulate so-called acute dilatation. We need greater accuracy in the use of this term and also much more investigation by exact methods as by the use of the teleroentgenograph or orthodiagraph, in the study of the heart throughout the course of an infectious disease. This is important work highly to be commended, for at present the subject is a very hazy one.

Prognosis in infectious disease based on cardiovascular symptoms, such as dyspnea and palpitation, and on many signs, such as tachycardia and relation of pulse-rate to blood-pressure, is liable to be misleading. Signs already mentioned of actual heart involvement are of course much more important.

Finally, I shall say a few words about the treatment of the heart and the circulation in infectious disease. Such therapy may be divided into three groups in the order of their importance: First, specific treatment of disease is most important. Of course this is possible only in certain diseases, but in those it must be accomplished with wisdom. By so doing much heart disease can be avoided and the progress of that already begun stopped. This is particularly true of diphtheria with antitoxin, and syphilis with arsphenamine and mercury. In rheumatic fever I feel convinced that the salicylates act almost as a specific. Certainly when given early in the disease and pushed the infection can usually be stopped short and by so doing probably much heart disease averted. This is a very important measure to urge, I believe, in the prophylaxis of rheumatic heart disease. It and tonsillectomy give us some hope for the future. In some other diseases such as pneumonia and meningitis, which once in a while attack the heart, we have to a certain extent specific antisera which would tend, by shortening the course of the disease, to prevent heart involvement.

Second in importance in the treatment and prevention of cardiac involvement in acute infectious disease is good nursing care. During the war, when often we were short of medical officers and very low in drugs, we found we got along surprisingly well if only we had good nurses. So in infectious disease, with or without heart involvement, the patient should be carefully nursed.

Finally, we have symptomatic drug therapy. Here is where the difficulty comes. Much of this treatment is empirical and there is great need for accurate and painstaking observation. I feel that much time and money have been wasted in giving all manner of "stimulating" drugs to patients with circulatory or general failure in infectious disease. Once in a while a patient seems to be tided over a crisis by this therapy, but nineteen others fail to respond. We are liable to feel, in our present state of knowledge, because of an occasional apparent successful response, that we should stick to it and fill every one with drugs. While working in a typhus epidemic in Eastern Macedonia two years ago a colleague of ours got typhus fever. The Greek military surgeons urged that they be allowed to treat him with frequent subcutaneous injections—caffein, camphor, adrenalin and strychnine. We objected and they warned us that he might die if he did not receive these drugs. We got two excellent American nurses, gave him no drugs and he had an early crisis, on the tenth or eleventh day, without complications. Of course such a case is of little moment except to show the present chaotic situation in regard to such therapy. We must get more light on these points so that our treatment will be more reasonable. One well-trained man gives digitalis as a routine to all patients with pneumonia, another decries it and gives none except as heart failure may be manifested. Which is right? This is an important question, for if we can prove that digitalis always helps in pneumonia we should always give it. On the other hand if it rarely helps and perhaps often makes more toxic, for it must be remembered that digitalis is a poison, when should we give it, if at all? Cohn and Jamieson[4] have shown that digitalis has an undoubted influence on a fever heart, but are we sure that this influence is a good one? T. Stuart Hart[5] has reported a study of digitalis action in bronchopneumonia, and he states that there was absolutely no difference in the course of the disease or the pulse-rate between the digitalized and the non-digitalized cases of bronchopneumonia, except in two cases of chronic cardiovascular disease with auricular fibrillation, which were much benefited. Extensive experiments of this sort are necessary not only with digitalis but with other drugs, such as caffein and camphor. Once upon a time, not so very long ago, strychnine and alcohol were prescribed very freely at the Massachusetts General Hospital in pneumonia and other infectious diseases. The medical generation coming along now in Boston has hardly heard of such therapy except as of historical interest. This may be wrong, but I do not believe it is. We are a people of fads and fancies, and it seems to me that just at present the fad is digitalis, as a routine to avert circulatory failure in infectious disease. I want to urge further study of this important question.

Summary. In conclusion, then, it may be said that the heart is affected in two ways in acute infectious disease: First by direct permanent damage to endocardium, myocardium, and pericardium, and second by temporary poisoning. For both of these conditions it is necessary, first, to combat the infection itself by specific therapy, if there is such, and by good nursing care. The symptomatic therapy of cardiovascular symptoms and signs in the prevention of failure is on a very uncertain basis at present and needs further investigation. The routine employment of digitalis in such infectious diseases as typhoid fever and pneumonia is unwarranted. Finally, the frequent occurrence of the effort syndrome during and following infectious disease and simulating at times cardiac disease is in need of emphasis.

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[4] Jour. Exper. Med., 1917, 25.

[5] Am. Jour. Med. Sc., 1919, 168; Jour. Am. Med. Assn., 1919, 78.